properties and the transfected cells migrated effectively through the Matrigel layer (D), similar to the metastatic MDA-435 cells (A).

Similar antisense molecules may be prepared from other members of the PAR family, such as PAR-2 (SEQ ID NO: 8) (Fig. 9), PAR-3 (SEQ ID NO: 9) (Fig. 10) and PAR-4 (SEQ ID NO: 10) (Fig. 11a).

REMARKS

Claims 1-19 are pending. The attached Appendix includes marked-up copies of each rewritten paragraph (37 C.F.R. §1.121(b)(1)(iii)).

The attached paper copy and computer-readable copy of the Sequence Listing are submitted in compliance with 37 C.F.R. §§1.821-1.825. The contents of the paper copy and the computer-readable copy of the Sequence Listing are the same.

Support for the information provided in the Sequence Listing can be found in the specification at, for example, page 5 and in Figures 1, 2, 9 and 11, and in new Figure 10 filed herewith. Figure 10 is being replaced in order to correct an inadvertent error that was introduced into the specification. In particular, current Figure 10 recites the murine DNA sequence of PAR-3, rather than the human DNA sequence of PAR-3, which was clearly intended. New Figure 10 recites the human DNA sequence of PAR-3. The human DNA sequence of PAR-3 was known in the art at the time the present application was filed. As evidence of this, attached is a printout of Accession No. U92971 of the NCBI database indicating that the human DNA sequence of PAR-3 was known in the art. Thus, including this sequence in Figure 10 does not introduce new matter into the specification. As a result, no new matter is added in the Sequence Listing.

Early and favorable consideration on the merits is respectfully requested.

Respectfully submitted,

James A. Oliff
Registration No. 27,075

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JAO:MLM/jca

Attachments:
Appendix
NCBI Database Printout
Sequence Listing (paper and computer-readable copies)
Request for Approval of Drawing Correction

Date: August 29, 2001

OLIFF & BERRIDGE, PLC
P.O. Box 19928
Alexandria, Virginia 22320
Telephone: (703) 836-6400

DEPOSIT ACCOUNT USE AUTHORIZATION
Please grant any extension necessary for entry;
Charge any fee due to our Deposit Account No. 15-0461

APPENDIX

Changes to Specification:

A Sequence Listing is added.

Page 5, lines 14-19:

1) The protease activated domains and hirudin binding domain:

	Nucleotides	
hPAR-1(ThR)	37-61.....	TLDPRSFLLRNPNDKYEPFWEDEEK (SEQ ID NO: 1)
hPAR-2	32-56.....	SSKGRSLIGKVDGTSHVTGKGVTVE (SEQ ID NO: 2)
hPAR-3	34-57.....	TLPIKTFRGAPPN SFEEFPFSALE (SEQ ID NO: 3)
hPAR-4	28-52.....	LPAPRGYPGQVCANDSDTHELPDSS (SEQ ID NO: 4)

Page 6, lines 1-3:

Fig. 1 shows the DNA (SEQ ID NO: 5) and amino acid sequence (SEQ ID NO: 6) of human ThR **[1]**;

Fig. 2 shows the DNA sequence of an antisense cDNA of ThR (SEQ ID NO: 7);

Fig. 3 shows the location of the ThR antisense in the pcDNA III vector;

Page 7, lines 24-26:

Fig. 9 shows the DNA sequence of PAR-2 (SEQ ID NO: 8);

Fig. 10 shows the DNA sequence of PAR-3 (SEQ ID NO: 9);

Fig. 11a shows the DNA sequence of PAR-4 (SEQ ID NO: 10);

Fig. 11b shows the amino acid sequence of PAR-4 (SEQ ID NO: 11). ~~and~~

Page 15, lines 4-20:

To analyze the impact of reduced ThR expression in the highly metastatic cells, MDA-435 breast carcinoma cells were transfected with an antisense ThR cDNA (SEQ ID NO: 7) mammalian expression vector containing ThR cDNA in an antisense orientation under the control of the Cytomegalovirus (CMV) promoter (see Figs. 2 and 3).

The vector alone was used as a control. Western blot analysis of ThR protein levels showed a marked reduction in the antisense transfected cells (Fig. 8, lane A) as compared to vector alone (lane B) or untreated MDA-435 cells (lane C). When the antisense transfected cells were tested in the Matrigel invasion assay, the otherwise aggressively invading cells showed a markedly reduced level of invasion, similar to that of the non-metastatic breast carcinoma cell line MCF-7 (Fig. 8, E&F). Transfection with the vector alone had no effect on the invasion properties and the transfected cells migrated effectively through the Matrigel layer (D), similar to the metastatic MDA-435 cells (A).

Similar antisense molecules may be prepared from other members of the PAR family, such as PAR-2 (SEQ ID NO: 8) (Fig. 9), PAR-3 (SEQ ID NO: 9) (Fig. 10) and PAR-4 (SEQ ID NO: 10) (Fig. 11a).